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* * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:05:29 ON 18 JUN 2001

=> file biosis medline caplus wpids uspat

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*** YOU HAVE NEW MAIL ***

=> s recombinant expression construct

L1          117 RECOMBINANT EXPRESSION CONSTRUCT

=> s l1 lysosomal enzyme

MISSING OPERATOR L1 LYSOSOMAL
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l1 and lysosomal enzyme

L2            2 L1 AND LYSOSOMAL ENZYME

=> s l2 and plant cell

L3            2 L2 AND PLANT CELL

=> d l3 bib abs 1-2


L3   ANSWER 1 OF 2  WPIDS COPYRIGHT 2001   DERWENT INFORMATION LTD
AN   1997-202248 [18]   WPIDS
DNN  N1997-167118       DNC C1997-064741
TI   Production of enzymatically active (modified) lysosomal
     enzyme in transgenic plants  - useful in treatment of lysosomal
     storage disorders.
```

CYC 75
PI WO 9710353 A1 [redacted] 970320 (199718)* EN 111p
RW: AT BE CH DE DK EA ES FI FP GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AU AZ BA BB BG BR BY CA CN CU CZ EE FI GE HU IL IS JP KG KP KR KZ LC LK LR LS LT LV MD MG MK MN MX NO NZ PL RO RU SG SI SK TJ TM TR TT UA UZ VN
AU 9670711 A 19970401 (199730)
EP 865499 A1 19980923 (199842) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 5929304 A 19990727 (199936)
ADT WO 9710353 A1 WO 1996-US14730 19960913; AU 9670711 A AU 1996-70711 19960913; EP 865499 A1 EP 1996-931569 19960913, WO 1996-US14730 19960913; US 5929304 A Provisional US 1995-3737 19950914, US 1996-713928 19960913
FDT AU 9670711 A Based on WO 9710353; EP 865499 A1 Based on WO 9710353
PRAI US 1995-3737 19950914; US 1996-713928 19960913
AN 1997-202248 [18] WPIDS
AB WO 9710353 A UPAB: 19970502
A novel method for producing an enzymatically active **lysosomal enzyme** (A) or modified **lysosomal enzyme** (B) in a transgenic plant, comprises: (a) growing the transgenic plant which has a **recombinant expression construct** comprising a nucleotide sequence encoding (A) or (B) and a promoter (preferably inducible promoter) that regulates expression of the nucleotide sequences so that (A) or (B) is expressed in the transgenic plant; and (b) recovering (A) or (B) from an organ of the transgenic plant; where (B) has the amino acid sequence of (A) with one or several amino acid substitutions, additions and/or deletions, and the organ is a leaf, stem, root, flower, fruit or seed. Also claimed are: (1) a **recombinant expression construct** (I) comprising a nucleotide sequence as above encoding (A) or (B); (2) a plant transformation vector comprising (I); (3) a **plant cell**, tissue or organ which has the recombinant expression vector of (2); (4) a transgenic plant or **plant cell** capable of producing (A) or (B) which contains a **recombinant expression construct** as in (1); and (5) (A) or (B) produced by growing a transgenic plant as in (4) and recovering the enzyme from an organ of the transgenic plant as above.

USE - The plant expression system provides for post-translational modification and processing to produce a recombinant gene product ((A) or (B)) exhibiting enzymatic activity. (A) and (B) are useful for enzyme replacement therapy for therapeutic treatment of human and animal lysosomal storage diseases, e.g. Fabry, Farber and Gaucher diseases and Tay-Sachs, and industrial processes involving enzymatic substrate hydrolysis.

Dwg.0/21

L3 ANSWER 2 OF 2 USPATFULL
AN 1999:85655 USPATFULL
TI Production of lysosomal enzymes in plant-based expression systems
IN Kadin, David N., Blacksburg, VA, United States
Cramer, Carole L., Blacksburg, VA, United States
Oishi, Karen K., Blacksburg, VA, United States
Weissenborn, Deborah L., Blacksburg, VA, United States
PA Croptech Development Corporation, United States (U.S. corporation)
Virginia Tech Intellectual Properties, Inc., United States (U.S. corporation)
PI US 5929304 19990727
AI US 1996-713928 19960913 (8)
PRAI US 1995-3737 19950914 (60)

ECL Exemplary Claim: 1
DRWN 34 Drawing Figure(s); 29 Drawing Page(s)
LN.CNT 2625
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to the production of enzymatically active recombinant human and animal lysosomal enzymes involving construction and expression of recombinant expression constructs comprising coding sequences of human or animal lysosomal enzymes in a plant expression system. The plant expression system provides for post-translational modification and processing to produce a recombinant gene product exhibiting enzymatic activity. The invention is demonstrated by working examples in which transgenic tobacco plants having recombinant expression constructs comprising human hGC and IDUA nucleotide sequences produced enzymatically active modified human glucocerebrosidase and human .alpha.-L-iduronidase. The recombinant lysosomal enzymes produced in accordance with the invention may be used for a variety of purposes, including but not limited to enzyme replacement therapy for the therapeutic treatment of human and animal lysosomal storage diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his

(FILE 'HOME' ENTERED AT 13:05:29 ON 18 JUN 2001)

FILE 'BIOSIS, MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 13:05:51 ON 18 JUN 2001

L1 117 S RECOMBINANT EXPRESSION CONSTRUCT
L2 2 S L1 AND LYSOSOMAL ENZYME
L3 2 S L2 AND PLANT CELL

=> s l1 and lysosomal

L4 3 L1 AND LYSOSOMAL

=> s l4 not l3

L5 1 L4 NOT L3

=> d l5 bib abs

L5 ANSWER 1 OF 1 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-638567 [61] WPIDS
DNN N2000-473642 DNC C2000-192121
TI Recombinant mammalian fibrosarcoma cell for identifying compounds that inhibit or potentiate cellular senescence, regulated by p21, comprises a **recombinant expression construct** encoding a p21 gene.
DC B04 D16 S03
IN CHANG, B; RONINSON, I B
PA (UNII) UNIV ILLINOIS FOUND
CYC 87
PI WO 2000061751 A1 20001019 (200061)* EN 119p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 2000040790 A 20001114 (200108)
ADT WO 2000061751 A1 WO 2000-US9286 20000407; AU 2000040790 A AU 2000-40790 20000407
FDT AU 2000040790 A Based on WO 200061751
PRAI US 1999-446583 19991129; US 1999-128676 19990409
AN 2000-638567 [61] WPIDS
AB WO 200061751 A UPAB: 20001128
NOVELTY - A recombinant mammalian fibrosarcoma cell (I) comprising a **recombinant expression construct** (II) encoding a mammalian p21 gene (III), where p21 is expressed in (I), is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) (I) comprising (II) encoding (III) transcriptionally controlled

(2) identifying a compound that inhibits p21-mediated modulation of cellular gene expression by expressing p21 in (I) and assaying (I) in the presence of the compound for a decrease in expression of cellular genes whose expression is modulated by p21;

(3) (I) comprising (II) encoding a reporter gene under the transcriptional control of a promoter for a mammalian gene whose expression is:

(a) modulated by p21 and (I) contains a second (II) encoding (III), where expression of p21 is experimentally-induced in (I);

(b) inhibited by p21 and the promoter is of the genes for ORC1, PRC1, XRCC9, CDC2, cyclin B1, AIK1, CENP-A, CENP-F, MAD2, BUBR1, MCAK, HSET, CHL1, thymopoietin alpha , MPP2, MPP5, CDC47/MCM7, CDC21/MCM4, DNA ligase I, DNA polymerase alpha , RAD54, exonuclease HEX1/RAD2, PLK1, dihydofolate reductase (DHFR) or citron kinase; or

(c) induced by p21 and the promoter is of the genes for serum amyloid A, complement C3, connective tissue growth factor, integrin beta -3, activin A, natural killer cell protein 4, prosaposin, Mac2 binding protein, galectin-3, superoxide dismutase 2, granulin/epithelin, p66shc, **lysosomal** beta -galactosidase, or cathepsin B;

(4) identifying a compound that inhibits p21-mediated modulation of cellular gene expression, by expressing p21 in (I) and assaying (I) for decreases in expression of the reporter gene;

(5) identifying a compound that inhibits senescence in (I) by treating (I) with an agent or culturing (I) to induce senescence, where (I) may comprise a reporter gene controlled by a promoter for a gene modulated by p21 and assaying (I) for a decrease in repression of induction of the genes;

(6) inhibiting cellular senescence by contacting (I) with an identified inhibitor;

(7) inhibiting production of disease associated gene products in (I), by contacting (I) with an identified inhibitor;

(8) identifying a compound that potentiates the effects of p21-mediated modulation of cellular gene expression by expressing p21 in (I) and assaying for increases in expression of cellular genes induced or repressed by p21;

(9) identifying a compound that potentiates senescence by contacting (I) with an agent or culturing (I) to induce senescence, where (I) comprises a reporter gene under the control of a promoter for a mammalian gene whose expression is modulated by p21 and assaying (I) for increases in expression of the reporter gene; and

(10) identifying a compound that promotes induction of senescence in (I) by treating (I) with an agent or culturing the cell to induce senescence in the presence of the compound and assaying (I) for increased repression or induction of genes by p21;

(11) identifying a compound that promotes induction of senescence in (I) by contacting (I) with an agent or culturing (I) to induce senescence, where (I) contains a reporter gene under the control of a promoter for a gene whose expression is modulated by p21 and assaying (I) for increased expression of the reporter gene;

(12) promoting senescence in (I) by contacting (I) with an identified compound;

(13) an identified compound that inhibits or potentiates p21 modulation of cellular gene expression or senescence

(14) producing an anti-apoptotic or mitogenic factor from a (I) by

progression by expressing p21 in (I), obtaining and comparing cellular mRNA from (I) before and after induction of p21;

(17) obtaining nucleic acid enriched for genes encoding secreted proteins with paracrine functions and proteins involved in senescence and age-related disease by expressing p21 in (I) and obtaining cellular mRNA from (I) before and after induction of p21;

(18) identifying cellular genes that are markers of senescence by expressing p21 in a population (P1) of (I) and quiescence in a second population (P2) of (I), obtaining mRNA from each population (I), comparing the pattern of gene expression in P1 before and after p21 is induced with the pattern in P2 before and after quiescence, and identifying the genes strongly induced in P1 and not in P2;

(19) detecting senescence in (I) by detecting expression of a gene for connective tissue growth factor, serum amyloid A, integrin beta -3, activin A, natural killer cell protein 4, Mac2 binding protein, or tissue transglutaminase;

(20) identifying a compound that induces senescence in (I) by assaying (I) for expression of a gene modulated by p21 and the compound is an inducer when there is an increase in repression or expression of a gene in the presence of the compound;

(21) identifying a compound that induces senescence in (I) by contacting (I), comprising a reporter gene under the control of a promoter for a gene modulated by p21, with the compound and assaying for induction of sensescence when expression of the reporter gene is reduced under the control of a promoter for a gene repressed by p21 or increased under the control of genes induced by p21;

(22) (II) encoding a reporter gene under the control of a promoter for a mammalian gene whose expression is inhibited or induced by p21; and

(23) inhibiting production of mitogenic or anti-apoptotic compounds in (I) comprising contacting (I) with an inhibitor.

USE - (I) is used in methods for identifying genes involved in cell cycle progression, growth promotion, modulation of apoptosis, cellular senescence and aging and for identifying compounds that inhibit or potentiate cellular senescence, regulated by p21 (claimed). (I) can be used to produce or an anti-apoptotic or mitogenic factor (claimed).

Dwg.0/10

=> s l5 and plant

L6 0 L5 AND PLANT

=> s l1 and plant cell

L7 14 L1 AND PLANT CELL

=> s l7 and enzyme

4 FILES SEARCHED...

L8 12 L7 AND ENZYME

=> dup rem l8

PROCESSING COMPLETED FOR L8

L9 12 DUP REM L8 (0 DUPLICATES REMOVED)

=> d l9 bib abs 1-12

TI Methods of delivery using cationic lipids and helper lipids
IN Wang, Jinkang, San Francisco, CA, United States
Zhang, Yi-Lin, San Mateo, CA, United States
PA Valentis, Inc., Burlingame, CA, United States (U.S. corporation)
PI US 6235310 B1 20010522
AI US 1998-54769 19980403 (9)
PRAI US 1997-88359 19970404 (60)
DT Utility
EXNAM Primary Examiner: Kishore, Gollamudi S.
LREP McDonnell Boehnen Hulbert & Berghoff
CLMN Number of Claims: 40
ECL Exemplary Claim: 1
DRWN 9 Drawing Figure(s); 9 Drawing Page(s)
LN.CNT 1164
AB Methods and compositions are provided for the introduction of polyanionic molecules, in particular, nucleic acids, into mammalian cells using certain phosphatidyl ethanolamines as helper lipids in conjunction with various cationic lipids. In particular, cationic lipid-mediated transfection of mammalian cells is improved by the use of lipid carriers comprising DLPE or DiPPE and cationic lipids.

L9 ANSWER 2 OF 12 USPATFULL
AN 2000:138504 USPATFULL
TI Nucleotide sequences that encode phosphatidylinositol-3' kinase associated proteins and uses thereof
IN Braselmann, Sylvia, San Francisco, CA, United States
PA Onyx Pharmaceuticals, Inc., Richmond, CA, United States (U.S. corporation)
PI US 6133419 20001017
AI US 1997-942008 19971001 (8)
PRAI US 1996-30103 19961101 (60)
DT Utility
EXNAM Primary Examiner: Achutamurthy, Ponnathapu; Assistant Examiner: Tung, Peter P.
LREP Giotta, Gregory
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1939
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Identification, characterization and expression of nucleotides that encode phosphatidylinositol-3' kinase associated protein(s) that bind to the intermediate SH2 domain on the regulatory subunit of PI3K, p85, by the associated protein(s) C-terminal amino acids, and that exhibit a bromodomain are described, as well as methods of using such proteins for medical applications, including diagnosis and treatment cell growth disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 3 OF 12 USPATFULL
AN 2000:9752 USPATFULL
TI G-beta-gamma regulated phosphatidylinositol-3' kinase
IN Stephens, Len, Sawston, United Kingdom
Hawkins, Phillip Thomas, Sawston, United Kingdom
Braselmann, Sylvia, San Francisco, CA, United States
PA Onyx Pharmaceuticals, Inc., Richmond, CA, United States (U.S.

RLI Continuation of Ser. No. US 1997-916917, filed on 15 Aug 1997, now patented, Pat. No. US 5856132 which is a continuation-in-part of Ser. No. US 1996-672211, filed on 27 Jun 1996, now patented, Pat. No. US 5874273
DT Utility
EXNAM Primary Examiner: Achutamurthy, Ponnathapu; Assistant Examiner: Slobodyansky, Elizabeth
LREP Pennie & Edmonds LLP, Giotta, Esq., Gregory
CLMN Number of Claims: 25
ECL Exemplary Claim: 1
DRWN 10 Drawing Figure(s); 21 Drawing Page(s)
LN.CNT 4917
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to the discovery, identification and characterization of nucleotides that encode the G protein regulated phosphatidylinositol-3' kinase, a heterodimeric **enzyme** which produces the intracellular messenger phosphatidylinositol (3,4,5)-triphosphate in response to activation of trimeric G protein-linked receptors. This novel protein, comprised of a catalytic subunit, p120, and a regulatory subunit, p101, is found in cells of hematopoietic origin and is involved in immune system responses which cause inflammation. The presence of p101 subunit is largely responsible for the dramatic stimulation of kinase activity in the presence of activated trimeric G proteins. The invention encompasses p101 and p120 nucleotides; host cell expression systems, p101 and p120 proteins, fusion proteins, polypeptides and peptides, antibodies to these proteins, transgenic animals that express a p101 or p120 transgene, or recombinant knock-out cells and animals that do not express the p101 or p120 gene, antagonists and agonists of the **enzyme**, and other compounds that modulate p101 or p120 gene expression or **enzyme** activity that can be used for diagnosis, drug screening, clinical trial monitoring, and/or the treatment of inflammatory disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 4 OF 12 USPATFULL
AN 1999:113557 USPATFULL
TI Methods of screening foods for nutraceuticals
IN Ghai, Geetha, Murray Hill, NJ, United States
Boyd, Charles, New Brunswick, NJ, United States
Csiszar, Katalin, New Brunswick, NJ, United States
Ho, Chi-Tang, East Brunswick, NJ, United States
Rosen, Robert T., Pottersville, NJ, United States
PA Rutgers, The State University of New Jersey, New Brunswick, NJ, United States (U.S. corporation)
PI US 5955269 19990921
AI US 1996-670826 19960620 (8)
DT Utility
EXNAM Primary Examiner: Myers, Carla J.
LREP Pennie & Edmonds LLP
CLMN Number of Claims: 43
ECL Exemplary Claim: 1
DRWN 1 Drawing Page(s)
LN.CNT 2155
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to an assay system for screening nutraceuticals, i.e., foods or food substances that occur naturally, or that are produced during processing which are capable of modulating in a subject the expression of one or more genes associated with a disease or undesirable physical condition. The nutraceuticals identified by the screening assays can be incorporated into compositions which may be

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 5 OF 12 USPATFULL
AN 1999:106321 USPATFULL
TI Modulators of BRCA1 activity
IN Rubinfeld, Bonnee, Danville, CA, United States
Polakis, Paul G., Mill Valley, CA, United States
Lingenfelter, Carol, Oakland, CA, United States
Vuong, Terilyn T., Oakland, CA, United States
PA Onyx Pharmaceuticals, Inc., Richmond, CA, United States (U.S. corporation)
PI US 5948643 19990907
AI US 1997-968751 19970813 (8)
DT Utility
EXNAM Primary Examiner: Hutzell, Paula K.; Assistant Examiner: Sun-Hoffman, Lin
LREP Giotta, Gregory
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN 5 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 2263
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions of matter consisting of a family of related nucleotide sequences that encode proteins, termed BRCA1 Modulator Proteins, that bind to the tumor suppressor gene product BRCA1, and methods of using the nucleotide sequences and the proteins encoded thereby, to diagnose and/or treat disease where the BRCA1 Modulator Proteins have an apparent
molecular weight of 45-97 kdaltons and are characterized by having at least one leucine zipper domain, and optionally a zinc finger domain.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 6 OF 12 USPATFULL
AN 1999:85655 USPATFULL
TI Production of lysosomal enzymes in plant-based expression systems
IN Padin, David N., Blacksburg, VA, United States
Cramer, Carole L., Blacksburg, VA, United States
Oishi, Karen K., Blacksburg, VA, United States
Weissenborn, Deborah L., Blacksburg, VA, United States
PA Croptech Development Corporation, United States (U.S. corporation)
Virginia Tech Intellectual Properties, Inc., United States (U.S. corporation)
PI US 5929304 19990727
AI US 1996-713928 19960913 (8)
PRAI US 1995-3737 19950914 (60)
DT Utility
EXNAM Primary Examiner: Kemmerer, Elizabeth
LREP Fennie & Edmonds LLP
CLMN Number of Claims: 73
ECL Exemplary Claim: 1
DRWN 14 Drawing Figure(s); 29 Drawing Page(s)
LN.CNT 2625
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to the production of enzymatically active recombinant human and animal lysosomal enzymes involving construction and expression of recombinant expression constructs comprising coding sequences of human or animal lysosomal enzymes in a plant expression system. The plant expression system provides for post-translational modification and processing to produce a recombinant gene product

produced enzymatically active modified human glucocerebrosidase and human .alpha.-[redacted]duronidase. The recombinant lysosomal enzymes produced in accordance with the invention may be used for a variety of purposes, including but not limited to **enzyme** replacement therapy for the therapeutic treatment of human and animal lysosomal storage diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 7 OF 12 USPATFULL
AN 1999:24494 USPATFULL
TI G-beta-gamma regulated phosphatidylinositol-3' kinase
IN Stephens, Len, Sawston, England
Hawkins, Philip Thomas, Sawston, England
PA Onyx Pharmaceuticals, Richmond, CA, United States (U.S. corporation)
PI US 5874273 19990223
AI US 1996-672211 19960627 (8)
DT Utility
EXNAM Primary Examiner: Patterson, Jr., Charles L.; Assistant Examiner: Slobodyansky, Elizabeth
LREP Pennie & Edmonds LLP
CLMN Number of Claims: 33
ECL Exemplary Claim: 1
DRWN 15 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 4148
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to the discovery, identification and characterization of nucleotides that encode the G protein regulated phosphatidylinositol-3' kinase, a heterodimeric **enzyme** which produces the intracellular messenger phosphatidylinositol (3,4,5)-triphosphate in response to activation of trimeric G protein-linked receptors. This novel protein, comprised of a catalytic subunit, p120, and a regulatory subunit, p101, is found in cells of hematopoietic origin and is involved in immune system responses which cause inflammation. The presence of p101 subunit is largely responsible for the dramatic stimulation of kinase activity in the presence of activated trimeric G proteins. The invention encompasses p101 and p120 nucleotides, host cell expression systems, p101 and p120 proteins, fusion proteins, polypeptides and peptides, antibodies to these proteins, transgenic animals that express a p101 or p120 transgene, or recombinant knock-out cells and animals that do not express the p101 or p120 gene, antagonists and agonists of the **enzyme**, and other compounds that modulate p101 or p120 gene expression or **enzyme** activity that can be used for diagnosis, drug screening, clinical trial monitoring, and/or the treatment of inflammatory disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 8 OF 12 USPATFULL
AN 1999:18940 USPATFULL
TI G-beta-gamma regulated phosphatidylinositol-3' kinase
IN Stephens, Len, Sawston, England
Hawkins, Phillip Thomas, Sawston, England
PA Onyx Pharmaceuticals, Richmond, CA, United States (U.S. corporation)
PI US 5869271 19990209
AI US 1997-972630 19971118 (8)
RLI Division of Ser. No. US 1996-672211, filed on 27 Jun 1996
DT Utility
EXNAM Primary Examiner: Wax, Robert A.; Assistant Examiner: Slobodyansky, Elizabeth
LREP Pennie & Edmonds LLP, Giotta, Gregory
CLMN Number of Claims: [illegible]

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to the discovery, identification and characterization of nucleotides that encode the G protein regulated phosphatidylinositol-3' kinase, a heterodimeric **enzyme** which produces the intracellular messenger phosphatidylinositol (3,4,5)-triphosphate in response to activation of trimeric G protein-linked receptors. This novel protein, comprised of a catalytic subunit, p120, and a regulatory subunit, p101, is found in cells of hematopoietic origin and is involved in immune system responses which cause inflammation. The presence of p101 subunit is largely responsible for the dramatic stimulation of kinase activity in the presence of activated trimeric G proteins. The invention encompasses p101 and p120 nucleotides, host cell expression systems, p101 and p120 proteins, fusion proteins, polypeptides and peptides, antibodies to these proteins, transgenic animals that express a p101 or p120 transgene, or recombinant knock-out cells and animals that do not express the p101 or p120 gene, antagonists and agonists of the **enzyme**, and other compounds that modulate p101 or p120 gene expression or **enzyme** activity that can be used for diagnosis, drug screening, clinical trial monitoring, and/or the treatment of inflammatory disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 9 OF 12 USPATFULL

AN 1999:4855 USPATFULL

TI G-beta-gamma regulated phosphatidylinositol-3' kinase

IN Stephens, Len, Sawston, England
Hawkins, Phillip Thomas, Sawston, England

PA Onyx Pharmaceuticals, Richmond, CA, United States (U.S. corporation)

PI US 5859201 19990112

AI US 1997-972629 19971118 (8)

RLI Division of Ser. No. US 1996-672211, filed on 27 Jun 1996

DT Utility

EXNAM Primary Examiner: Wax, Robert A.; Assistant Examiner: Slobodyonsky, Elizabeth

LREP Pennie & Edmonds LLP, Giotta, Gregory

CLMN Number of Claims: 13

ECL Exemplary Claim: 1

DRWN 15 Drawing Figure(s); 14 Drawing Page(s)

LN.CNT 4012

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to the discovery, identification and characterization of nucleotides that encode the G protein regulated phosphatidylinositol-3' kinase, a heterodimeric **enzyme** which produces the intracellular messenger phosphatidylinositol (3,4,5)-triphosphate in response to activation of trimeric G protein-linked receptors. This novel protein, comprised of a catalytic subunit, p120, and a regulatory subunit, p101, is found in cells of hematopoietic origin and is involved in immune system responses which cause inflammation. The presence of p101 subunit is largely responsible for the dramatic stimulation of kinase activity in the presence of activated trimeric G proteins. The invention encompasses p101 and p120 nucleotides, host cell expression systems, p101 and p120 proteins, fusion proteins, polypeptides and peptides, antibodies to these proteins, transgenic animals that express a p101 or p120 transgene, or recombinant knock-out cells and animals that do not express the p101 or p120 gene, antagonists and agonists of the **enzyme**, and other compounds that modulate p101 or p120 gene expression or **enzyme** activity that can be used for diagnosis, drug screening, clinical trial monitoring, and/or the treatment of inflammatory disorders.

TI G-beta-gamma r[illegible]lated phosphatidylinositol-3'k[illegible]se
IN Stephens, Len, [illegible]mbridge, England
Hawkins, Phillip Thomas, Cambridge, England
PA Onyx Pharmaceuticals, Richmond, CA, United States (U.S. corporation)
PI US 5856133 19990105
AI US 1997-972631 19971118 (8)
RLI Division of Ser. No. US 1996-672211, filed on 27 Jun 1996
DT Utility
EXNAM Primary Examiner: Wax, Robert A.; Assistant Examiner: Slobodyansky, Elizabeth
LREP Pennie & Edmonds and Gregory Giotta LLP
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN 15 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 3974
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to the discovery, identification and characterization of nucleotides that encode the G protein regulated phosphatidylinositol-3'kinase, a heterodimeric **enzyme** which produces the intracellular messenger phosphatidylinositol (3,4,5)-triphosphate in response to activation of trimeric G protein-linked receptors. This novel protein, comprised of a catalytic subunit, p120, and a regulatory subunit, p101, is found in cells of hematopoietic origin and is involved in immune system responses which cause inflammation. The presence of p101 subunit is largely responsible for the dramatic stimulation of kinase activity in the presence of activated trimeric G proteins. The invention encompasses p101 and p120 nucleotides, host cell expression systems, p101 and p120 proteins, fusion proteins, polypeptides and peptides, antibodies to these proteins, transgenic animals that express a p101 or 120 transgene, or recombinant knockout cells and animals that do not express the p101 or p120 gene, antagonists and agonists of the **enzyme**, and other compounds that modulate p101 or p120 gene expression or **enzyme** activity that can be used for diagnosis, drug screening, clinical trial monitoring, and/or the treatment of inflammatory disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 11 OF 12 USPATFULL
AN 1999:1471 USPATFULL
TI G-beta-gamma regulated phosphatidylinositol-3' kinase
IN Stephens, Len, Sawston, England
Hawkins, Phillip Thomas, Sawston, England
Braselmann, Sylvia, San Francisco, CA, United States
PA Onyx Pharmaceuticals, Richmond, CA, United States (U.S. corporation)
PI US 5856132 19990105
AI US 1997-916917 19970815 (8)
RLI Continuation-in-part of Ser. No. US 1996-672211, filed on 27 Jun 1996
DT Utility
EXNAM Primary Examiner: Wax, Robert A.; Assistant Examiner: Slobodyansky, Elizabeth
LREP Pennie & Edmonds LLP, Giotta, Gregory
CLMN Number of Claims: 42
ECL Exemplary Claim: 1
DRWN 22 Drawing Figure(s); 21 Drawing Page(s)
LN.CNT 4569
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to the discovery, identification and characterization of nucleotides that encode the G protein regulated phosphatidylinositol-3' kinase, a heterodimeric **enzyme** which produces the intracellular messenger phosphatidylinositol

cause inflammation. The presence of p101 subunit is largely responsible for the dramatic stimulation of kinase activity by the presence of activated trimeric G proteins. The invention encompasses p101 and p120 nucleotides, host cell expression systems, p101 and p120 proteins, fusion proteins, polypeptides and peptides, antibodies to these proteins, transgenic animals that express a p101 or p120 transgene, or recombinant knock-out cells and animals that do not express the p101 or p120 gene, antagonists and agonists of the **enzyme**, and other compounds that modulate p101 or p120 gene expression or **enzyme** activity that can be used for diagnosis, drug screening, clinical trial monitoring, and/or the treatment of inflammatory disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 12 OF 12 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1997-202248 [18] WPIDS
DNN N1997-167118 DNC C1997-064741
TI Production of enzymatically active (modified) lysosomal **enzyme** in transgenic plants - useful in treatment of lysosomal storage disorders.
DC B04 C06 D16 P13
IN CRAMER, C L; OISHI, K K; RADIN, D N; WEISSENBORN, D L
PA (CROP-N) CROPTECH DEV CORP; (VIRG) VIRGINIA TECH INTELLECTUAL PTY INC; (VIRG) VIRGINIA TECH INTELLECTUAL PROPERTIES
CYC 75
PI WO 9710353 A1 19970320 (199718)* EN 111p
FW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AU AZ BA BB BG BR BY CA CN CU CZ EE FI GE HU IL IS JP KG KP KR KZ LC LK LR LS LT LV MD MG MK MN MX NO NZ PL RO RU SG SI SK TJ TM TR TT UA UZ VN
AU 9670711 A 19970401 (199730)
EP 865499 A1 19980923 (199842) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 5929304 A 19990727 (199936)
ADT WO 9710353 A1 WO 1996-US14730 19960913; AU 9670711 A AU 1996-70711 19960913; EP 865499 A1 EP 1996-931569 19960913, WO 1996-US14730 19960913; US 5929304 A Provisional US 1995-3737 19950914, US 1996-713928 19960913
FDT AU 9670711 A Based on WO 9710353; EP 865499 A1 Based on WO 9710353
PRAI US 1995-3737 19950914; US 1996-713928 19960913
AN 1997-202248 [18] WPIDS
AB WO 9710353 A UPAB: 19970502
A novel method for producing an enzymatically active lysosomal **enzyme** (A) or modified lysosomal **enzyme** (B) in a transgenic plant, comprises: (a) growing the transgenic plant which has a **recombinant expression construct** comprising a nucleotide sequence encoding (A) or (B) and a promoter (preferably inducible promoter) that regulates expression of the nucleotide sequences so that (A) or (B) is expressed in the transgenic plant; and (b) recovering (A) or (B) from an organ of the transgenic plant; where (B) has the amino acid sequence of (A) with one or several amino acid substitutions, additions and/or deletions, and the organ is a leaf, stem, root, flower, fruit or seed. Also claimed are: (1) a **recombinant expression construct** (I) comprising a nucleotide sequence as above encoding (A) or (B); (2) a plant transformation vector comprising (I); (3) a **plant cell**, tissue or organ which has the recombinant expression vector of (2); (4) a transgenic plant or **plant cell** capable of producing (A) or (B) which contains a **recombinant expression construct**

USE - The plant expression system provides for post-translational modification and processing to produce a recombinant gene product ((A) or (B)) exhibiting enzymatic activity. (A) and (B) are useful for **enzyme** replacement therapy for therapeutic treatment of human and animal lysosomal storage diseases, e.g. Fabry, Farber and Gaucher diseases and Tay-Sachs, and industrial processes involving enzymatic substrate hydrolysis.

Dwg.0/21

=> s recombinant construct

L10 537 RECOMBINANT CONSTRUCT

=> s l10 and lysosomal enzyme

L11 2 L10 AND LYSOSOMAL ENZYME

=> s l11 not l3

L12 2 L11 NOT L3

=> s l12 and plant cell

L13 2 L12 AND PLANT CELL

=> d l13 bib abs 1-2

L13 ANSWER 1 OF 2 USPATFULL
AN 96:111347 USPATFULL
TI Cloning and expression of biologically active .alpha.-galactosidase A as
a fusion protein
IN Desnick, Robert J., New York, NY, United States
Bishop, David F., New York, NY, United States
Ioannou, Yiannis A., New York, NY, United States
PA The Mount Sinai School of Medicine of the City University of New York, New York, NY, United States (U.S. corporation)
PI US 5580757 19961203
AI US 1994-261577 19940617 (8)
RLI Division of Ser. No. US 1992-983451, filed on 30 Nov 1992, now patented, Pat. No. US 5401650 which is a continuation-in-part of Ser. No. US 1990-602824, filed on 24 Oct 1990, now patented, Pat. No. US 5356804 And
Ser. No. US 1990-602608, filed on 24 Oct 1990, now patented, Pat. No. US
5382524
DT Utility
EXNAM Primary Examiner: Wax, Robert A.; Assistant Examiner: Hendricks, Keith D.
LREP Pennie & Edmonds
CLMN Number of Claims: 15
ECL Exemplary Claim: 5
DRWN 51 Drawing Figure(s); 38 Drawing Page(s)
LN.CNT 3138
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention involves the production of large quantities of human .alpha.-Gal A by cloning and expressing the .alpha.-Gal A coding sequence in eukaryotic host cell expression systems. The eukaryotic expression systems, and in particular the mammalian host cell expression
system described herein provide for the appropriate cotranslational and

Using the meth[redacted] described herein, the recomb[redacted]t .alpha.-Gal A is secreted by the engineered host cells so that it is recovered from the culture medium in good yield. The .alpha.-Gal A produced in accordance with the invention may be used, but is not limited to, in the treatment in Fabry Disease; for the hydrolysis of .alpha.-galactosyl residues in glycoconjugates; and/or for the conversion of the blood group B antigen on erythrocytes to the blood group O antigen.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 2 OF 2 USPATFULL
AN 95:27218 USPATFULL
TI Cloning and expression of biologically active .alpha.-galactosidase A
IN Desnick, Robert J., New York, NY, United States
Bishop, David F., New York, NY, United States
Ioannou, Yiannis A., New York, NY, United States
PA The Mount Sinai School of Medicine of the City University of New York, New York, NY, United States (U.S. corporation)
PI US 5401650 19950328
AI US 1992-983451 19921130 (7)
RLI Continuation-in-part of Ser. No. US 1990-602824, filed on 24 Oct 1990 And Ser. No. US 1990-602608, filed on 24 Oct 1990
DT Utility
EXNAM Primary Examiner: Wax, Robert A.; Assistant Examiner: Hendricks, Keith D.
LREP Pennie & Edmonds
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 51 Drawing Figure(s); 38 Drawing Page(s)
LN.CNT 3083
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention involves the production of large quantities of human .alpha.-Gal A by cloning and expressing the .alpha.-Gal A coding sequence in eukaryotic host cell expression systems. The eukaryotic expression systems, and in particular the mammalian host cell expression
system described herein provide for the appropriate cotranslational and posttranslational modifications required for proper processing, e.g., glycosylation, phosphorylation, etc. and sorting of the expression product so that an active enzyme is produced. In addition, the expression of fusion proteins which simplify purification is described.

Using the methods described herein, the recombinant .alpha.-Gal A is secreted by the engineered host cells so that it is recovered from the culture medium in good yield. The .alpha.-Gal A produced in accordance with the invention may be used, but is not limited to, in the treatment in Fabry Disease; for the hydrolysis of .alpha.-galactosyl residues in glycoconjugates; and/or for the conversion of the blood group B antigen on erythrocytes to the blood group O antigen.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d l12 kwic

L12 ANSWER 1 OF 2 USPATFULL
SUMM 10.1.1. Construction Of Plasmids For **Lysosomal Enzyme** Overproduction
DETD Efforts to express this enzyme in eukaryotic expression systems were [illegible]

DETD . . . a sequence may either be co-transfected into the host cell along with the gene of interest, or included in the **recombinant construct** encoding the gene of interest. Alternatively, cell lines containing this sequence may be produced which are then transfected with the. . .

DETD . . . it appears that the protein A domain does not interfere with either the folding or the proper processing of this **lysosomal enzyme**. Furthermore, the presence of the dimerized .alpha.-Gal A polypeptide did not inhibit the binding of the protein A domain to. . .

DETD . . . synthesis and is secreted 45-60 min later. These fast kinetics of recombinant .alpha.-Gal A biosynthesis allow for interesting studies involving **lysosomal enzyme** biosynthesis and offer a methodology that, to date, is only rivaled by viral systems. In fact, recombinant .alpha.-Gal A is. . .

DETD . . . in the antisense orientation, nor in the cells that received no DNA. In addition, the .beta.-galactosidase levels, determined as a **lysosomal enzyme** control, were not changed (FIG.2B).

DETD TABLE IV

Lysosomal Enzyme Activities Secreted In Culture Media Of Transfected CHO Cells		
	CHO Cell Line	
Lysosomal Enzyme	DG44* Control	5-3.sub.250 * .alpha.-Gal A
.alpha.-Galactosidase A	56	16,900
.alpha.-Arabinosidase		

. . .

DETD 10.1.1. CONSTRUCTION OF PLASMIDS FOR **LYSOSOMAL ENZYME** OVERPRODUCTION

DETD . . . to efficiently characterize the biosynthesis, posttranslational modifications, and mechanisms responsible for the lysosomal targeting and selective secretion of this prototype **lysosomal enzyme**, thereby providing further insight into the nature of protein transport and sorting in mammalian cells.

=> d l12 2 kwic

L12 ANSWER 2 OF 2 USPATFULL

SUMM 10.1.1. Construction Of Plasmids For **Lysosomal Enzyme** Overproduction

DETD Efforts to express this enzyme in eukaryotic expression systems were equally difficult for different reasons. The .alpha.-Gal A is a **lysosomal enzyme** encoded by a "housekeeping" gene. The primary translation product is highly modified and processed, requiring a complex series of events. . .

DETD . . . a sequence may either be co-transfected into the host cell along with the gene of interest, or included in the **recombinant construct** encoding the gene of interest. Alternatively, cell lines containing this sequence may be produced which are then transfected with the. . .

DETD . . . it appears that the protein A domain does not interfere with either the folding or the proper processing of this **lysosomal enzyme**. Furthermore, the presence of the dimerized .alpha.-Gal A polypeptide did not inhibit the binding of the protein A domain to. . .

methodology th[redacted] to date, is only rivaled by v[redacted]l systems. In fact, recombinant .al[redacted]a.-Gal A is. . .

DETD . . . in the antisense orientation, nor in the cells that received no

DNA. In addition, the .beta.-galactosidase levels, determined as a **lysosomal enzyme** control, were not changed.

DETD TABLE IV

Lysosomal Enzyme Activities Secreted In Culture Media Of Transfected CHO Cells

	CHO Cell Line	
	DG44*	5-3.sub.250 *
Lysosomal Enzyme	Control	.alpha.-Gal A
.alpha.-Galactosidase A	56	16,900
.alpha.-Arabinosidase	2.4	0.9
.alpha.-Fucosidase	341	358
.beta.-Galactosidase	35.2	8.9
.beta.-Gaucuronidase	90.0	53.7
.beta.-Hexosaminidase	2,290	2,090
.alpha.-Mannosidase	147	82.8
Acid Phosphatase	30.6. . .	

DETD 10.1.1. CONSTRUCTION OF PLASMIDS FOR **LYSOSOMAL ENZYME** OVERPRODUCTION

DETD . . . to efficiently characterize the biosynthesis, post-translational modifications, and mechanisms responsible for the lysosomal targeting and selective secretion of this prototype **lysosomal enzyme**, thereby providing further insight into the nature of protein transport and sorting in mammalian cells.